

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 12 MAY 2005

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To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2005/000445

International filing date (day/month/year)
13.01.2005

Priority date (day/month/year)
30.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07C219/28, C07C57/145, C07C51/41, A61K31/222, A61P27/08

Applicant
AZIENDE CHIMICHE RIUNITE ANGELINI FRANCESCO ...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Authorized Officer

Zervas, B

Telephone No. +31 70 340-3667



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000445

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2005/000445

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims	1-11
	No: Claims	
Inventive step (IS)	Yes: Claims	1-11
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following documents:

- D1: WO 90/04964 A (ZAMBON GROUP S.P.A.) 17 May 1990 (1990-05-17)
D2: WO 86/03970 A (SIMES, SOCIETA ITALIANA MEDICINALI E SINTETICI, S.P.A.) 17 July 1986 (1986-07-17)
D3: CASAGRANDE C. ET AL.: "Synthesis and chemical properties of Ibopamine and or related esters of N-substituted dopamines- Synthesis of Ibopamine metabolites." ARZNEIMITTEL FORSCHUNG. DRUG RESEARCH., vol. 36, no. 2a, 1986, pages 291-303, XP000926659 DEEDITIO CANTOR. AULENDORF.

1. Novelty

The present application does meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 - 11 is new in the sense of Article 33(2) PCT.

None of the relevant prior art documents D1 - D3 disclose the maleate salt of ibopamine nor its preparation and its use. The documents D1 and D2 disclose both the hydrochloride of ibopamine, whereas D3 discloses and the hydrochloride, the hydrobromide, the acid tartrate and the succinate of ibopamine.

2. Inventive Step

The present application does also meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 - 11 does involve an inventive step in the sense of Article 33(3) PCT.

The document D1, which discloses ophthalmic compositions containing ibopamine hydrochloride is regarded as representing the closest prior document. In view of D1 the problem underlying the present application can be defined as providing improved ibopamine salts which are useful in ophthalmic compositions. The applicant has solved the problem in providing the maleate of ibopamine, which has a better ocular tolerability than the hydrochloride. Consequently, an inventive step underlying the subject-matter of claims 1 to 11 can be acknowledged.

**WRITTEN OPINION OF THE
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AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2005/000445

3. Industrial Applicability

The subject-matter of claims 1 - 11 is industrial applicable.